DETAILED ACTION

Currently, Claims 27-29, 31-44, 48-50, and 52 are pending. Claims 27-29, 35-37, 39, 41-44, 48-50, and 52 and examined on the merits. Claims 1-26, 30, 45-47, and 51 are canceled. Claims 31-34, 38, and 40 are withdrawn.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections - 35 USC § 112

As previously rejected, Claims 35-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Undue experimentation would be required to practice the invention as claimed due to the quantity of experimentation necessary; limited amount of guidance and limited number of working examples in the specification; nature of the invention; state of the prior art; relative skill level of those in the art; predictability or unpredictability in the art; and the breadth of the claims. In re Wands, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Limited amount of guidance and limited number of working examples in the specification

While the Specification recited a composition of matter derivable from Aloe vera or a plant or an animal extract (page 2, lines 10-11), there is no indication as to how NAG-25 is made. Applicant indicated that NAG-25 stands for no affinity for Sephadex G-25 (page 3, lines 28); however, the processes by which the composition is made cannot be determined because of the ambiguity surrounding the extraction protocol discussed on pages 21-22 which is explained in detail below:

Page 21 indicates that aloe extracts and reconstituted powders were placed over a Sephadex G-25 column. The Aloe extracts used for these experiments are undefined. Page 20 indicates that many different extracts were used such as AV-1 to Av-7, AV-15, AV-16 and AV-A to AV-F. Therefore, it appears that at least 15 extracts were subjected to the subfractionation protocol discussed on page 21. The Examiner does not know what these extracts are or if they are available to the public. Although Applicants state that "[a]ll of these products were Aloe inner gel fillet products. These gel fillets were prepared as described in CA patent No. 1305475" it is unclear how the extracts were originally prepared and what sources these originated from . Even if Applicants were to provide evidence that these extracts are known and readily available and that one of skill in the art would be able to read the extracts of the specification; e.g., AV-1 and be able to determine what extract this is and where to obtain them, the confusion surrounding making NAG-25 would still remain:

The protocol of pp.21-22 indicates: 'Fraction III, also indicated as Aloe vera NAG-25 extract, see hereunder.' So, it appears in this section, that NAG-25 is made by placing an extract of Aloe vera over Sephadex G25. However, page 22 under 'Aloe vera NAG-25 extract' indicates: 10 gram spray dried Aloe vera spray dried extract originating from 2 liter Aloe vera extract was solubilized…passed over a Sephadex G-25 column…Aloe vera NAG-25 is collected as the 60-310 ml eluate." It is unclear first, what Aloe extract is used to make NAG-25, out of the 15 that were subjected to the purification protocol (it appears that all of the extracts may have been subjected separately to purification protocols although, the extracts may have been pooled- the Examiner is guessing that the extracts were treated separately, but the specification does not clearly state as such). Secondly, on page 21 under 'subfractionation' the aloe extracts and reconstituted powders were centrifuged and only the supernatant was used which was first passed over a 0.2 micrometer membrane prior to purification over a Sephadex G-25 column. There is no mention of centrifuging or filtering the extract under the NAG-25 protocol on page 22.

Therefore, it is unclear how to make NAG-25. Absent clear indication of how to go about making NAG-25 the skilled artisan could not reproduce this composition.

Predictability or unpredictability in the art

Because there are many ways to make and concentrate an extract, the unpredictability in the art would be high.

Applicant argues that page 21, lines 13-19 describes all the necessary steps for preparation of NAG-25 extract from Aloe gel extracts, aloe vera extracts are commercial products and available to the public, the company Bioclin is a commercial source.

In response to Applicant's argument, the Applicant's Specification indicated more than 15 extracts for aloe vera were subjected to the subfractionation protocol discussed on page 21. The Examiner does not know what these extracts are or if they are available to the public. Commercial source changes with time and one does not know whether the same extract is being produced. Specification should be amended to clear up the confusion.

Claim Rejections - 35 USC § 103

Claims 27-29, 35-37, 39, 41-44, 48-50, and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yaron et al. (1992, J Agric Food Chem, 40: 1316-1320) in view of Hart et al. (1989, Planta Medica, 55: 509-512) for the reasons set forth in the previous Office Action, which is set forth below. All of Applicant's arguments regarding this ground of rejection have been fully considered but are not persuasive.

For the purposes of searching for and applying prior art under 35 U.S.C. 102 and 103, absent a clear indication in the specification or claims of what the basic and novel

characteristics actually are, "consisting essentially of" will be construed as equivalent to "comprising." See, e.g., PPG, 156 F.3d at 1355, 48 USPQ2d at 1355 ("PPG could have defined the scope of the phrase consisting essentially of' for purposes of its patent by making clear in its specification what it regarded as constituting a material change in the basic and novel characteristics of the invention."). See also > AK Steel Corp. v. Sollac, 344 F.3d 1234, 1240-41, 68 USPQ2d 1280, 1283-84 (Fed. Cir. 2003) (Applicant's statement in the specification that "silicon contents in the coating metal should not exceed about 0.5% by weight" along with a discussion of the deleterious effects of silicon provided basis to conclude that silicon in excess of 0.5% by weight would materially alter the basic and novel properties of the invention. Thus, "consisting essentially of" as recited in the preamble was interpreted to permit no more than 0.5% by weight of silicon in the aluminum coating). MPEP 2111.03.

Thus, the claims can still be interpreted as reading, “comprising”.

Yaron et al. teaches use of aloe vera in cosmetic formulation and in health foods (Introduction, paragraph 1) and polysaccharide profile of aloe vera gel comprises 60.2% mannose, 22.2% glucose, 1.6% galactose (Table I). The anionic polysaccharides have significantly higher viscosity and yield point (page 1318, left column, paragraph 1). Aloe vera is a plant. Aloe vera inherently has anti-bacterial or anti-inflammatory effects. Aloe gel is used in topical treatment of injure skin and in digestive tract (Introduction, paragraph 1). Fresh aloe gel was dialyzed to remove low molecular weight sugars and quinones (page 1316, Chemical Anaylsis). The isolated aloe vera would consist of the

negatively charged polysaccharides from aloe vera. Anionic polysaccharides could serve to preserve aloe vera gel (page 1319, right column, last paragraph).

However, Yaron et al. does not teach 60-90% mannose, 30-10% glucose, 1-10% monosaccharide, 100-300 MW, separation on anion-exchange chromatography, tablet, capsule and syrup, an injectable dosage.

Hart et al. teaches an immunomodulatory substance from aloe vera leaves, where the extract is fractionated by anion-exchange chromatography and gel filtration to yield polysaccharides, at 320,000 MW and 200,000 MW, in BI, which contains 92.1% mannose, 3.2% glucose, 3.8% galactose, and 0.9% arabinose; BII, which contains 83.7% mannose, 8.8% galactose, 3.9% glucose and 3.6% arabinose (page 510, Results). Aloe vera polysaccharide can have glucose/mannose ratios ranging from 1:5.1 to 1:19 (page 512, Discussion). The range from 1:5.1 and 1:19 is about 1:5 and 1:20. Anion-exchange column will isolate negative charge polysaccharides because the column is positively charged. Chromatography is a form of ultrafiltration. Aloe can be used to treat bacterial infection (Introduction, paragraph 1). Low molecular weight constituents do not have modulation of complement activity (page 510, Result, paragraph 1).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition comprising 60-90% mannose, 30-10% glucose, 1-10% monosaccharide, 100-300 MW of the active agent combination for the following reasons. Hart et al. teaches an immunomodulatory substance from aloe vera leaves, where the extract at 320,000 MW and 200,000 MW, in BI, which contains 92.1%

mannose, 3.2% glucose, 3.8% galactose, and 0.9% arabinose; BII, which contains 83.7% mannose, 8.8% galactose, 3.9% glucose and 3.6% arabinose (page 510, Results). Aloe vera polysaccharide can have glucose/mannose ratios ranging from 1:5.1 to 1:19 (page 512, Discussion). The range from 1:5.1 and 1:19 is about 1:5 and 1:20. Yaron et al. teaches polysaccharide profile of aloe vera gel comprises 60.2% mannose, 22.2% glucose, 1.6% galactose (Table I). Thus, it would have been obvious to make a concentrated composition containing mannose, glucose, galactose for use as a supplement to the diet.

Additionally, the amount of a specific ingredient in a composition that is used for a particular purpose (the composition itself or that particular ingredient) is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Thus, optimization of general conditions is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results, especially within the ranges taught by the reference. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to isolate higher molecular weight polysaccharides because low molecular weight polysaccharides do not have activity (see Hart et al.). One would have been motivated to make polysaccharides with higher molecular weight isolates for the expected benefit of biological active polysaccharides from aloe vera as taught by Yaron et al. and Hart et al. Absent evidence to the contrary, there would have been a reasonable expectation of success in making the claimed invention from the combined teachings of the cited references.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use aloe vera as a cosmetic or food because Yaron et al. teaches use of aloe vera in cosmetic formulation and in health foods (Introduction, paragraph 1) and Hart et al. teaches an immunomodulatory substance from aloe vera leaves. One would have been motivated to make aloe vera for cosmetic and food uses for the expected benefit of immunomodulatory effect of aloe vera. Absent evidence to the contrary, there would have been a reasonable expectation of success in making the claimed invention from the combined teachings of the cited references.

The references also do not specifically teach formulating the composition in the tablet, capsule and syrup, and injectable forms claimed by applicant. These pharmaceutical forms are well known in the art to be acceptable means of administering a pharmaceutically active substance. Based on this knowledge, a person of ordinary skill in the art would have had a reasonable expectation that formulating the composition taught by the references in the claimed forms would be successful.

Therefore, an artisan of ordinary skill would have been motivated to formulating the composition taught by the reference in the forms claimed by applicant.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to make a composition consisting of 70-90% D-mannose and 30-10% D-glucose, and 0-10% monosaccharide and polysaccharides have an average molecular weight of about 100-300 kD. Yaron et al. teaches that aloe gel polysaccharide composition varies upon production conditions and because aloe gels are known to contain the same sugars as claimed and are known to be purified from aloe having similar molecular weights and sugar profiles, that absent any evidence that the aloe gel of the claims displays any unexpected result over the aloe gel of the prior art, that the claimed invention appears to be an obvious variation of known aloe products. Thus, it would have been obvious to make a concentrated composition containing 70-90% D-mannose and 30-10% D-glucose, and 0-10% monosaccharide and posaccharides have an average molecular weight of about 100-300 kD for use as a supplement to the diet, topical use, and injection. Additionally, the amount of a specific ingredient in a composition that is used for a particular purpose (the composition itself or that particular ingredient) is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955). Thus, optimization of general conditions is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary

for an artisan of ordinary skill to determine the optimal amount of each ingredient to add in order to best achieve the desired results, especially within the ranges taught by the reference. Thus, absent some demonstration of unexpected results from the claimed parameters, this optimization of ingredient amount would have been obvious at the time of applicant's invention.

Applicant argues that Yaron and Hart do not teach the particular polysaccharide fraction from Aloe vera that has improved curative properties.

In response to Applicant's argument, the claims are drawn toward aloe vera extract with negative charges, molecular weight higher than 50 kDa, with 60-90% mannose, 30-10% D-glucose, and 0-10% other monosaccharides. Yaron teaches Aloe vera inherently has anti-bacterial or anti-inflammatory effects. Aloe gel is used in topical treatment of injure skin and in digestive tract (Introduction, paragraph 1). Hart et al. teaches an immunomodulatory substance from aloe vera leaves, where the extract is fractionated by anion-exchange chromatography and gel filtration to yield polysaccharides, at 320,000 MW (320 kDa) and 200,000 MW (200 kDa), in BI, which contains 92.1% mannose, 3.2% glucose, 3.8% galactose, and 0.9% arabinose; BII, which contains 83.7% mannose, 8.8% galactose, 3.9% glucose and 3.6% arabinose (page 510, Results). Aloe vera polysaccharide can have glucose/mannose ratios ranging from 1:5.1 to 1:19 (page 512, Discussion). The range from 1:5.1 and 1:19 is about 1:5 and 1:20. Anion-exchange column will isolate negative charge

polysaccharides because the column is positively charged. Thus, curative properties, with molecular weight higher than 50 kDa, negative charged ale vera extract is taught.

Applicant argues that Yaron teaches mixture of aloe vera with other exogenous sources.

In response to Applicant's argument, the claim language is interpreted to be "comprising"; therefore, other exogenous sources mixed with aloe vera read on the claims.

Applicant argues that the polysaccharide described by Hart is different from the claimed polysaccharide.

In response to Applicant's argument, the ratio of Aloe vera polysaccharide can have glucose/mannose ratios ranging from 1:5.1 to 1:19 (page 512, Discussion). The range from 1:5.1 and 1:19 is about 1:5 and 1:20. Anion-exchange column will isolate negative charge polysaccharides because the column is positively charged. Hart et al. teaches an immunomodulatory substance from aloe vera leaves, where the extract is fractionated by anion-exchange chromatography and gel filtration to yield polysaccharides, at 320,000 MW (320 kDa) and 200,000 MW (200 kDa). There is not much difference in the characteristic of the aloe vera claimed and the one taught by Hart. Aloe vera inherently has antimicrobial activities, thus, there is no unexpected characteristics.

Applicant argues that there is no reason to optimize the experimental condition.

In response to Applicant's argument, Hart teaches Aloe vera polysaccharide can have glucose/mannose ratios ranging from 1:5.1 to 1:19 (page 512, Discussion). The 0% monosaccharide would not be with the ratio. Thus, the percentages of glucose to mannose can be extrapolated from the ratio ranges. Thus, routine experimental optimization would be probable to obtain particular glucose/mannose concentrations to achieve an aloe vera extract for a particular purpose.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CATHERYNE CHEN whose telephone number is

(571)272-9947. The examiner can normally be reached on Monday to Friday, 9-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Terry McKelvey can be reached on 571-272-0775. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Catheryne Chen
Examiner Art Unit 1655

/PATRICIA A LEITH/
Primary Examiner, Art Unit 1655